(3) *Requests for certification; samples.* In addition to complying with the requirements of §431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, sterility, pyrogens, moisture, pH, penicillin G content, and crystallinity.

(ii) Samples required:

(*a*) For all tests except sterility: 10 packages, each containing approximately 300 milligrams.

(*b*) For sterility testing: 20 packages, each containing approximately 600 milligrams.

(b) *Tests and methods of assay*—(1) *Potency.* Use either of the following methods; however, the results obtained from the iodometric assay shall be conclusive.

(i) *Microbiological agar diffusion assay.* Proceed as directed in §436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately measured representative portion of the sample in sufficient absolute methyl alcohol to give a solution of convenient concentration. Immediately, further dilute with 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to the reference concentration of 1.0 unit of penicillin G per milliliter (estimated).

(ii) *Iodometric assay.* Proceed as directed in §436.204 of this chapter.

(2) *Sterility.* Proceed as directed in §436.20 of this chapter, using the method described in paragraph (e)(2) of that section, except use medium C in lieu of medium A, medium F in lieu of medium E, and during the period of incubation shake the tubes at least once daily.

(3) *Pyrogens.* Proceed as directed in §436.32(d) of this chapter, using a solution containing 4,000 units of penicillin G per milliliter.

(4) [Reserved]

(5) *Moisture.* Proceed as directed in §436.201 of this chapter.

(6) *pH.* Proceed as directed in §436.202 of this chapter, except prepare the sample as follows: Dissolve 50 milligrams of sample with 50 milliliters of absolute ethyl alcohol. Add 50 milliliters of distilled water and mix well.

(7) *Penicillin G content.* Accurately weigh approximately 50 milligrams of the sample, dissolve in absolute methyl alcohol, and dilute to 100 milliliters with absolute methyl alcohol. Treat a portion of the working standard in the same manner. Using a suitable spectrophotometer equipped with a quartz cell and absolute methyl alcohol as the blank, determine the absorbance at 263 nanometers. Calculate the percent penicillin G as follows:

$$\text{Percent penicillin G} = \frac{\text{Absorbance of sample} \times \text{weight in milligrams of standard} \times \text{percent penicillin G in standard}}{\text{Absorbance of standard} \times \text{weight in milligrams of sample}}$$

(8) *Crystallinity.* Proceed as directed in §436.203(a) of this chapter.

[42 FR 59858, Nov. 22, 1977, as amended at 45 FR 16472, Mar. 14, 1980; 49 FR 6092, Feb. 17, 1984; 50 FR 19918, 19919, May 13, 1985]

§440.71 Penicillin V.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Penicillin V is 3,3-dimethyl - 7-oxo-6-(2-phenoxyacetamido)-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid. It is so purified and dried that:

(i) Its potency is not less than 1,525 units nor more than 1,780 units per milligram.

(ii) [Reserved]

(iii) Its moisture content is not more than 2.0 percent.

(iv) Its pH in a saturated aqueous solution is not less than 2.5 and not more than 4.0.

(v) Its penicillin V content is not less than 90 percent and not more than 105 percent.

(vi) It is crystalline.

(2) *Labeling.* In addition to the labeling requirements of §432.5 of this chapter, each package shall bear on its outside wrapper or container and the immediate container the statement ''For

use in the manufacture of nonparenteral drugs only.''

(3) *Requests for certification; samples.* In addition to complying with the requirements of §431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, moisture, pH, penicillin V content, and crystallinity.

(ii) Samples required: 10 packages, each containing approximately 300 milligrams.

(b) *Tests and methods of assay*—(1) *Potency.* Assay for potency by any of the following methods; however, the results obtained from the bioassay method shall be conclusive.

(i) *Microbiological agar diffusion assay.* Proceed as directed in §436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample (approximately 30 milligrams) in 2.0 milliliters of absolute methyl alcohol. Further dilute an aliquot of this solution with sufficient 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to the reference concentration of 1.0 unit of penicillin V per milliliter (estimated).

(ii) *Iodometric assay.* Proceed as directed in §436.204 of this chapter.

(iii) *Hydroxylamine colorimetric assay.* Proceed as directed in §436.205 of this chapter.

(2) [Reserved]

(3) *Moisture.* Proceed as directed in §436.201 of this chapter.

(4) *pH.* Proceed as directed in §436.202 of this chapter, using a saturated aqueous solution prepared by adding approximately 30 milligrams per milliliter.

(5) *Penicillin V content.* Accurately weigh approximately 20 milligrams of the sample, dissolve in absolute methanol, and make to 100 milliliters with absolute methyl alcohol. Treat a portion of the working standard in the same manner. Using a suitable spectrophotometer equipped with a quartz cell and absolute methyl alcohol as the blank, determine the absorbance of the peak at 276 nanometers. Calculate the percent penicillin V as follows:

$$\text{Percent penicillin V} = \frac{\text{Absorbance of sample} \times \text{weight in milligrams of standard} \times \text{Percent penicillin V in standard}}{\text{Absorbance of standard} \times \text{Weight in milligrams of sample}}$$

(6) *Crystallinity.* Proceed as directed in §436.203(a) of this chapter.

[42 FR 59859, Nov. 22, 1977, as amended at 50 FR 19918, 19919, May 13, 1985]

§ 440.73 Penicillin V potassium.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Penicillin V potassium is the potassium salt of 3,3-dimethyl-7-oxo-6-(2-phenoxyacetamido) - 4 -thia - 1 - azabicyclo[3.2.0]heptane - 2 - carboxylic acid. It is so purified and dried that:

(i) Its potency is not less than 1,380 units nor more than 1,610 units per milligram.

(ii) [Reserved]

(iii) Its loss on drying is not more than 1.5 percent.

(iv) Its pH in an aqueous solution containing 30 milligrams per milliliter is not less than 4.0 and not more than 7.5.

(v) Its penicillin V content is not less than 81.2 percent and not more than 94.7 percent.

(vi) It is crystalline.

(2) *Labeling.* In addition to the labeling requirements of §432.5 of this chapter, each package shall bear on its outside wrapper or container and the immediate container the statement ''For use in the manufacture of nonparental drugs only.''

(3) *Requests for certification; samples.* In addition to complying with the requirements of §431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, loss on drying, pH, penicillin V content, and crystallinity.

(ii) Samples required: 10 packages, each containing approximately 300 milligrams.